



Activity 5

Making Decisions in the Face of Uncertainty

Focus: Students analyze a CD-ROM-based case study about a family's decisions related to testing for particular genetic variations that increase susceptibility to breast cancer and consider how understanding the related science can help people make decisions in uncertain circumstances.

At a Glance

Major Concepts: Our growing understanding of human genetic variation will allow us to identify genes that are associated with common diseases such as cancer. Genetic testing to identify individuals who have variations that make them susceptible to certain diseases can help people make decisions in uncertain circumstances and holds the prospect for more effective prevention and treatment. However, this capability also raises difficult questions that illustrate the personal and social implications of biological research.

Objectives: After completing this activity, students will

- recognize that our understanding of science can help us analyze and make decisions in uncertain circumstances;
- understand that the ability to identify susceptible individuals through genetic screening and testing holds the prospect for more effective prevention and treatment;
- understand that our ability to identify individuals susceptible to particular diseases also raises difficult questions about the uses of genetic information;
- be able to explain that although it is possible to analyze these questions rationally and civilly, people still may disagree on the answers; and
- understand that science can tell us what we can and cannot do, but we depend on an analysis of ethics and public policy (informed by a sound understanding of the science) to help determine what we should do.

Prerequisite Knowledge: Students should understand that cancer is characterized by uncontrolled growth of cells. Students also should understand that all cancer is fundamentally genetic because it results from the loss of genetic control of the cell cycle. That does not mean that all cancer is hereditary. The form of breast cancer that this activity addresses is one of the hereditary cancers, but it is responsible for only about 5 percent of all breast cancers. Most breast cancers arise from somatic mutations and thus are not hereditary.

Basic Science-Health Connection: This activity highlights the remarkable progress scientists are making in identifying genes related to multifactorial diseases such as cancer and focuses students' attention on the implications such discoveries have for personal health and decision making.

Introduction

This activity offers students the opportunity to apply their understanding of human genetic variation to a fictional case study involving a potentially painful set of decisions that various members of a family have to make. Teams of students analyze the case of a woman, Beth, who is concerned that she may carry a variant of either the *BRCA1* or *BRCA2* gene that predisposes to breast cancer. The case study is presented in five segments during which Beth makes two key decisions: (1) to proceed with being tested for altered forms of these genes and (2) after she develops cancer in one breast, not to have a prophylactic mastectomy of the other breast. Students analyze each segment by discussing a set of questions related to the underlying science and to the ethical and policy dilemmas raised by the decisions.

The activity's fundamental purpose is to help students see that an understanding of science and a clear, systematic analysis of options can help us make decisions in uncertain circumstances. Beth has a family history of breast cancer, a form of cancer that kills more than 40,000 women in the United States each year. Information about the presence of the altered gene could help her and her physician be more alert to the possibilities of her developing cancer.

On the other hand, she already is practicing the guidelines recommended to increase the chance of early detection should cancer develop. Furthermore, as students learn, breast cancer related to the presence of an inherited altered gene accounts for only 5 percent of the new cases of breast cancer diagnosed each year, and even if Beth is shown *not* to carry the altered gene, a certain risk of breast cancer remains. Thus, the decision whether to be tested is complex and is made more so by uncertainty related to the normal human genetic variation that exists among humans. Our understanding of genetic factors that can predispose individuals to certain cancers, while increasing, still is far from complete. The question about whether Beth should request prophylactic mastectomy of both breasts after she develops cancer in one breast is equally complex.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 5.1, *Analyzing the Issues* (make 1 copy per student)
- *Human Genetic Variation* CD-ROM (1 per team)

Follow the instructions on page 23 to load the CD-ROMs on the computers the students will use.

Note to teachers: If you do not have enough computers equipped with CD-ROM drives to conduct this activity, you can use the print-based alternative. To view and print the instructions and masters for this alternate activity, load the CD onto a computer and click the Print button on the main menu screen. The computer will display a screen showing the resources available for printing from the CD; click on the button labeled Non-CD Lesson Plan from the choices available for Activity 5, *Making Decisions in the Face of Uncertainty*. This will reveal the lesson plan and the masters for the alternate, non-CD-based lesson. Click Print again to print these resources.

Tip from the field test. Teachers who tested this activity raised two cautions.

- Students became so engaged in Beth's story that they lost sight of the major messages about genetic variation and its relationship to complex disease. Remind your students that Beth's difficult decisions arise because of progress in basic science that allows us to detect such genetic variations.
- Students tended to confuse the test for mutations in the *BRCA1* and *BRCA2* genes with a test for cancer itself. Be sure to clarify this distinction. The genetic test identifies forms of the *BRCA1* and *BRCA2* genes that can increase one's likelihood of developing cancer. It is not a test for cancer.

1. Open the activity by asking students whether they know anyone who has had breast cancer. Invite those students who wish to briefly describe their relationship to the individual involved to do so.

With approximately 1 in 8 American women developing breast cancer in their lifetimes, it would not be unusual for one or more of your students to be involved personally with this type of cancer. It may be that the student's mother or another family member has had or currently has cancer. For some of those students, discussions of cancer may be disturbing. We suggest that you watch your students for signs of discomfort (for example, tearfulness, reluctance to begin the activity, unusual silence or reticence) and provide appropriate support.

2. Direct students to organize into their teams and watch the CD-ROM-based videos *Making Decisions in the Face of Uncertainty* (the total running time is about 10 minutes). This first time through, ask students simply to watch and listen so they can get a sense of the complete case.

3. Distribute one copy of Master 5.1, *Analyzing the Issues*, to each student and explain that now the class will view the videos again, one segment at a time. Suggest that students take notes and list questions that occur to them as they watch each segment, then respond to the related questions on *Analyzing the Issues*. Discuss each segment in turn, as students complete it, using the questions on *Analyzing the Issues* as a guide. Address any other questions the students raise as well.

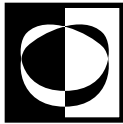
If students raise questions about the science or legal/policy issues that you and they cannot answer with the materials provided, suggest that someone pursue those answers outside of class.

Segment 1: Considering the Test

Question 1 What decision does Beth have to make?

Beth has to decide whether to have the test for mutations in her *BRCA1* and *BRCA2* genes. Your students might be interested in the financial aspects of the test. As of mid-1999, when this program was written, the laboratory cost for the combined test for *BRCA1* and *BRCA2* was about

Procedure



The identification of mutations that predispose individuals carrying them to cancer is an excellent example of how basic research in science yields results that benefit society. As students complete the activity, challenge them to think about the benefits that Beth and her family gain as a result of this knowledge. Ask students to summarize their ideas as you close the activity in Step 4.

\$2,500. The costs for the associated genetic counseling were about \$250 to \$300. Insurance coverage varies depending on the carrier.

Question 2 Who might be affected by Beth's decision?

Beth, her husband, her mother, her sisters, her teenage daughter, and her daughter's future husband (if she marries).

Question 3 What arguments support having the test?

This is a good opportunity to make certain that the students understand the underlying science in this case study. Files in the *Reference Database* on the CD-ROM will help students learn about the science. Students can access those files on their own, if you have enough CD-ROM players, or you can print the materials and distribute them.

Beth no longer will be uncertain about her status with respect to *BRCA1* and *BRCA2*. She will be able to make some other decisions, and she will be able to inform other family members about whether they are at risk for carrying a mutated form of one of the genes. Note that Beth says, with respect to a potentially negative genetic test, "You find out that you're safe." Ask students to comment on this remark. Emphasize that this test identifies only one type of risk factor for breast cancer. Simply because one does not have the particular mutations identified in this test does not mean that one "is safe" from developing breast cancer. There likely are other unknown genetic variations that can increase one's risk. Furthermore, only a small proportion of breast cancer is hereditary. Beth's comment about birth control pills provides an opportunity to discuss the constantly changing nature of scientific knowledge and to point out the environmental contributions to cancer.

Question 4 What arguments support *not* having the test?

Beth may not want to know. She also will not have to worry about whether she should share potentially positive test results with other members of the family. She will not have to make tough decisions about detection and/or prevention options (for example, prophylactic mastectomy), none of which is 100 percent effective.

Question 5 What factors do you think Beth and Charlie should consider in making their decisions?

Answers will vary, but be alert for misconceptions about the underlying science.

Segment 2: A Family Question

Question 1 What new facts have you learned about breast cancer?

In testing for genes related to cancer, it is helpful to test a family member who already has had the disease. Not all cancers are hereditary. The form of cancer that Beth's mother has may not be hereditary. If it is hereditary, it may be associated with a gene not yet identified by scientists.

Question 2 What are some of the family issues that arise in this counseling session?

Beth's mother feels guilty about her breast cancer and about the possibility that she has passed on the associated mutation. The issue of blame also arises, as well as the question of what Beth will do with the information if the test is positive. Note that the counselor stresses the importance of privacy and confidentiality. Emphasize for your students that genetic counselors are trained to handle the social and emotional aspects of counseling as well as the scientific aspects.

Question 3 What reasons does the genetic counselor give for not testing Jennifer? Do you agree that children under 18 should not be tested?

The counselor's reasons are rather nonspecific, simply that "teenagers often have different perspectives about developing breast cancer." Students' views on the testing of children under 18 will vary. Insist, however, that they provide concrete explanations for their positions and be alert to misunderstandings of the science.

The decision for a health care provider to conduct a genetic test is based on a variety of factors. Health care professionals are trained to reduce risks to their patients, including psychosocial risks. Anxiety and depression may arise in response to a positive test. A similar issue received attention in the mid-1980s, when health care professionals had to decide how to handle testing for exposure to the AIDS virus, HIV. At that point, the connection between a positive test for exposure to HIV and development of the fatal disease AIDS was not yet clear (although the correlation has since been established to the satisfaction of virtually all scientists). Keep in mind that not everyone who inherits an altered form of *BRCA1* or *BRCA2* develops breast cancer; thus, knowing that one carries such an allele may trigger needless anxiety.

Other factors that a health care provider considers when discussing genetic testing include the following questions:

- Can the related disorder, once diagnosed, be treated? In some cases, for example, Huntington disease, there are no treatments currently available that can help a person who tests positive.
- Does the patient exhibit symptoms, or is the order for a test based on family history alone?
- Do the benefits outweigh the harm brought about by knowledge of the test results?

The issue becomes even more complex when the patient to be tested is a minor, that is, under 18 years of age. The request for a genetic test may come from the parents or from the minor. When the minor is an

adolescent, the issue becomes particularly complicated because the patient may exhibit a considerable degree of autonomy regarding his or her health care decisions. Experts agree that in these cases the primary goal of genetic testing should be to promote the child's well-being. For example, the child who tests positive may be overindulged or may be treated as a scapegoat. Both of these problems can occur, however, even in the absence of testing. The testing of a child (or indeed any other family member) also has implications for all members of the family. In some cases, this forewarning will be welcomed; in others, it may be unwanted. Genetic testing of a child will ease some aspects of uncertainty, but people differ greatly in their response to such news.

In the case of genetic testing for mutations in the *BRCA1* gene, most health care providers and genetic testing centers adhere to a policy that denies tests to minors. This denial extends to requests from the parents, who are the legal guardians of the child's health. The psychological effects can be mixed. Whereas some individuals prefer the release from uncertainty, others could view a positive result as a death sentence and react in ways that are destructive to themselves or their families. Genetic testing requires informed consent, and some geneticists argue that this requirement automatically rules out children, and even teenagers, who generally are judged incapable of providing such consent. This view of minors, however, may be far too broad and may not be realistic. Some specialists are beginning to recognize that some adolescents and young children have sufficient autonomy in consent and decision making to make such decisions, and recommend that the desires of these youths should be taken into account. In any event, one must weigh the *balance* of potential harm and benefit in reaching a decision about testing a minor.

One outcome of the current policy is to delay the decision to test until the individual is an adult and can make the decision, rather than letting parents remove this option by making the choice themselves. Note that a *change* in policy most likely would result in *parents* being permitted to make the decision, rather than leaving the decision to the minor in question. Either way, issues of ethical decision making will arise.

Question 4 Beth's mother says, "I'm not sure more information is better." Do you agree with her? Explain your answer.

Answers will vary.

Segment 3: The Test Results

Question 1 Beth and her mother have had the genetic test. What new information have we learned?

Beth and her mother are positive for the *BRCA1* mutation. Beth has a lifetime risk of perhaps about 60 percent of developing breast cancer. This number is down from original estimates, which were as high as 87 percent. Some recent data suggest an even lower risk figure than 60

percent. In fact, as is often true when a new medical test becomes available, the exact figure is still not yet known. Further, it appears that the exact risk figure may vary, depending upon the exact mutation in the *BRCA1* that an individual woman carries.

Students also have learned that Beth may *not* develop breast cancer even though her test was positive and that Beth can do a number of things (breast self-examinations and mammograms, for example) to help detect any cancer early and, therefore, to begin early treatment.

Remember to emphasize that Beth and her mother were tested for mutations in the *BRCA1* and *BRCA2* genes, not for cancer.

Segment 4: A Diagnosis of Breast Cancer

Question 1 What new information have we learned about Beth?

It is now three years after the genetic test, and Beth has been diagnosed with cancer in one breast. There is a high risk of cancer in the other breast.

Question 2 What major decisions do Beth and her husband discuss in this segment?

First, they discuss whether Beth should have both breasts removed, and second, they consider whether to tell Jennifer that she is at risk for the *BRCA1* mutation. Note that even removal of both breasts does not guarantee that the cancer will not appear elsewhere or even appear in the remaining breast tissue.

Question 3 What do you think Beth and Charlie should do? Why?

Answers will vary, but make certain that students provide sound explanations for their positions. Again, make sure that the science is correct.

Segment 5: Jennifer's Decision

Question 1 What new information emerges in this segment?

Beth has had a lumpectomy, and Jennifer has not been tested. Emphasize that the chance of survival increases with early diagnosis.

Question 2 What is Jennifer's primary concern about the test?

She is concerned that potential employers and insurers will discriminate against her if they find out she has a high relative risk for breast cancer.

Question 3 Do you think employers or insurers should be able to deny employment or insurance to a person who has a genetic predisposition to a disease such as cancer? Explain your position.

Answers will vary. Inform students that at present many states have laws that prohibit health insurers from accessing and using genetic information in a discriminatory way. In addition, the federal Health

Insurance Portability and Accountability Act (HIPAA) prohibits those who issue commercial, employer-based, group health plans from discriminating against individuals on the basis of information gained from genetic tests.

Regarding employment discrimination, the Equal Employment Opportunity Commission extends “Americans with Disabilities” protection to individuals who experience discrimination based on genetic information related to illness, disease, or other disorders.

4. Close the activity by challenging students to identify the questions that now face Jennifer, Beth’s daughter, about her own health and personal welfare. Encourage students to think deeply about these questions. For each question that they identify as facing Jennifer, have them determine her options and begin to identify arguments that she might use in support of choosing one option over the other. Invite neighboring teams to discuss these questions. Then, use the following questions to stimulate a brief, final class discussion about the activity.



Use students’ answers to these questions to assess their understanding of the activity’s major concepts.

- Our understanding of and ability to identify genetic differences among us has increased remarkably in the last few decades and continues to increase. How might Beth’s and Jennifer’s decisions have been different 50 years ago? What advantages does our knowledge of human genetic variation bring us? What questions does it also raise?

Fifty years ago, Beth and Jennifer would not have been faced with the decision about whether to have these genetic tests. They would have had the option of lumpectomy or radical mastectomy if cancer were discovered. Our increased knowledge of human genetic variation has improved our understanding of the relationship between certain variations and disease and enabled us to test for some of these genetic variations. New knowledge and abilities, however, raise questions about whether we should test and about what we should do with the resulting information. The ability to test also raises the question of whether we should or will come to treat people who are genetically predisposed to illness as if they already are sick, even if they are not and may never be. These people are sometimes referred to as the “asymptomatically ill.” Ask the students to react to that designation.

- How does this activity illustrate the old saying that knowledge plus choice equals power?

The more we learn about a given situation—for example, our status with respect to the *BRCA1* and *BRCA2* genes—the greater our ability is to make decisions and control our own destiny, so long as the choices are available. The importance of choices emerges in this activity in at least two ways. First, Beth and Jennifer must be confident that information that results from the test will not be used against them. Otherwise they may feel, as Jennifer does, that they are not



Insist that students apply the saying to this activity. Then, to close the module effectively, ask students to apply the saying to our growing knowledge of human genetic variation (in general). Students should see that this knowledge offers us new opportunities and choices, but it also brings new challenges.

really free to choose whether to have the test. Second, the general policy not to test children under 18 for mutations in the *BRCA1* or *BRCA2* genes has restricted the choices for people under 18. This limits their access to knowledge about themselves and restricts their power to make decisions about their own lives.

Extend this activity by challenging students to connect what they learned in Activity 5 with what they learned in the two preceding activities. For example, ask students to connect Activity 5 with Activity 3 by suggesting how discovering mutations that predispose people to the development of cancer might help scientists develop new approaches to treating cancer. Then, assign students to learn more about this question by reading the article “Making headway against cancer” by J. Rennie & R. Rusting in the September 1996 special edition of *Scientific American*.

Likewise, connect Activity 5 with Activity 4 by asking students to research how discovering mutations that predispose people to the development of colon cancer has led to the creation of screening and counseling programs that are already saving lives by alerting people to their increased risk and helping them make good lifestyle and health care choices.

Potential Extensions